McAlister (Alex.)

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BY

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REPRINTED FROM THE

New York Medical Journal

for September 25, 1897.

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DIPHTHERIA ANTITOXINE.*

By ALEXANDER McALISTER, M. D.,
CAMDEN, N. J.

But little attention was given by the profession to the subject of diphtheria antitoxine before the meeting of the Eighth International Congress of Hygiene and Demography at Budapest, Hungary, in September, 1894, when Roux presented a paper reporting five hundred cases treated with antitoxine. Since then the remedy has been extensively used and reported upon in every civilized country. Recommended by the great body of laboratory workers, indorsed by thousands of physicians both in hospital and private practice, and welcomed by the common sense of the people at large, antitoxine has become the most widely indorsed and most generally employed of all remedies. Though confronted from the first by the fiercest opposition and materially retarded by the unbridled enthusiasm of some of its advocates, diphtheria antitoxine has within the brief period of three years proved itself to be specific in the full sense of that term.

* Read before the New Jersey State Medical Society, at Atlantic City, June 23, 1897.

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Emmett Holt, in his new text-book on *Diseases of Infancy and Childhood*, says: "Antitoxine is a specific remedy for experimental diphtheria in animals. Experience is now sufficient to justify the statement that it is specific in man, and just in the degree in which we can fulfill the conditions which are essential in experimental diphtheria" (folio 999). And again: "Gratifying as were the earlier results with the serum treatment, they have been constantly improving, and there is every reason to believe that, with larger experience both in the preparation and use of antitoxine, still better results will yet be reached. Certainly there is no remedy for any disease that has more testimony in its favor than has now diphtheria antitoxine" (folio 1000). These statements, which are fully indorsed by all the leading authorities, it will be noted, were made prior to the completion of the rich experience had with the remedy last winter, and before the results of the supplementary collective investigation of the American Pædiatric Association were made known, of which the *Medical News* of May 15, 1897, said editorially: "There can be no longer any doubt as to the value of the antitoxine treatment in all forms of diphtheria. The highest commendation should be accorded the American Pædiatric Association for so persistently adding line upon line, precept upon precept, until a verdict of *proved* has been established beyond peradventure. The final word has been spoken, a fact is before us."

The above-mentioned collective investigation showed that under antitoxine treatment seventy-three per cent. of operative cases of laryngeal diphtheria ended in recovery, and that only thirty-nine per cent. of cases so treated required operation. Under calomel treatment

only twenty-seven per cent. of the patients recovered, and ninety per cent. required intubation.

It is interesting to note how many eminent men in the profession and prominent medical magazines, after openly opposing antitoxine or treating it with stolid indifference, have joined the ranks of its advocates. Among many others Virchow "yielded to the brute force of figures," deeming it ignoble to face facts in brutish obstinacy; and Jacobi, who for twenty years has been a leading American authority on diphtheria, now finds in the failure to employ antitoxine in all cases of diphtheria a heavy shade of criminal neglect. The *Medical Record*, commenting upon the first report of the American Pædiatric Association, July 4, 1896, said: "The great majority of the profession may properly continue the use of antitoxine, but the great silent, careful, powerful jury of the profession is not yet ready with its final verdict." Commenting upon the second report of the American Pædiatric Association, May 15, 1897, the *Record* said: "The report is worthy of close study. Laryngeal diphtheria requiring operative interference furnishes the best test of the method of treatment. As the report mentions, before the days of antitoxine the best statistics could show only twenty-seven per cent. recovery. Other factors remaining constant, the use of antitoxine has carried the percentage from twenty-seven per cent. recovery up over the divide till it now reads twenty-seven per cent. mortality, nearly threefold increase in recoveries."

The deliberations of the American Medical Association, in its recent convention in Philadelphia, served to show how generally antitoxine is employed in the United States. The experiences of the last nine months, both

in the employment of the remedy and the collective study of results, have been such, and the evidence in its favor so overwhelmingly conclusive, that in a body of medical men, such as convened at Philadelphia, the physician who shows an aversion to the remedy has his motive for so doing and his sincerity immediately put in question. Every legitimate objection to the remedy is fully overcome in the employment of concentrated antitoxine, which was introduced during the spring of 1896 by the H. K. Mulford Company, Philadelphia, and which is now generally indorsed. The question to raise is how to employ the remedy in order to obtain the largest possible results. It is this phase of the present status of the serum treatment of diphtheria that is of most vital importance. The superiority of the antitoxine treatment of diphtheria over all other treatments can no longer be reasonably questioned, while the methods by which the fullest possible specific effects of the remedy may be secured are not everywhere well appreciated. The supplementary collective investigation showed that many physicians, rendered timid by the glaring headlines in yellow journalism, administered doses having from one tenth to one half the required number of antitoxic units. The results were proportionately unsatisfactory. The indications are that when a reliable product is employed generally in proper doses, repeated if need be within twelve hours, the general mortality from diphtheria will be reduced to less than four per cent. and that of laryngeal diphtheria to less than ten per cent.

Regarding the opposition, it has been well said that there are to-day in the whole civilized world not more than three or four active opponents of the antitoxine treatment of diphtheria whose names were known to

the profession before the introduction of antitoxine. While these have raised a great hue and cry, it is well to remember that they do not constitute the medical profession nor create truth. There can be no virtue in opposition which persists in the face of impregnable figures and established facts. That the fear of untoward results from an injection of antitoxine which some physicians still entertain is utterly groundless, is a patent fact in view of the countless injections already made in all parts of the civilized world, the number aggregating probably upward of two millions. In this large number it is admitted that five deaths occurred which could not be satisfactorily explained. They can not be proved, on the other hand, to have been caused by the antitoxine. In all the extensive laboratory researches nothing has yet been discovered which could possibly or probably contaminate the antitoxic serum and result in sudden death when administered. In the five cases referred to, in three of which immunizing doses were given, untoward symptoms appeared immediately upon injection of part or all of the serum, and death followed in from five to eight minutes. Virile germs, ptomaines, etc., even when nurtured in artificial media, are not capable of such results in small animals, much less in human beings. The cases simply remain unexplained for want of sufficient data. The remote cause was not recognized, and death was incidental to the injection—fear, probably, being the exciting cause.

Sudden deaths have always been a possible outcome of the diphtheritic infection, and, inasmuch as the severity of the infection is not always appreciated, it may be presumed that in some of these instances the disease

was not given the full share of blame. In the three instances cited causes other than the antitoxic serum must be sought for satisfactory explanations. In the early days of hypodermic medication sudden deaths were attributed to the use of the needle. Even to this day some communities will not tolerate the employment of hypodermic syringes. Quinine had its reported fatalities when first introduced. The coal-tar derivatives, now so extensively employed, have been credited with deaths, so have morphine, ether, chloroform, alcohol, and many other standard remedies. It is questionable whether one of these medicaments, within the prescribed doses, has a record nearly as clean as that of diphtheria antitoxine—viz., more than a million injections and only five deaths—which, to say the most, can not be satisfactorily explained. If it be conceded that there is an element of risk in the employment of antitoxine, this must be placed at one two-thousandth of one per cent., while the gain in recoveries ranges from twenty-five to thirty per cent. over all older treatments. If it is possible to give too large a dose of antitoxine, this limit has not yet been discovered. Rosenthal has given as high as six thousand units in a single injection. In one case which he reported, fifteen thousand units, and in another sixteen thousand five hundred units were administered during the continuance of the disease without untoward effects. Every case was followed by recovery. Dr. Sanor * reports the case of an infant nine days old successfully treated with concentrated antitoxine, "potent," twelve hundred and fifty units being used within twenty-four hours—five hundred at 10 A. M., five hundred at 6 P. M., and

* Dr. D. G. Sanor, Malvern, Ohio.

two hundred and fifty at 9 A. M. The case was grave; the throat and nose were full of exudate. The infant began to nurse at 2 P. M.

Within the prescribed range of doses diphtheria antitoxine may now be administered with the same degree of confidence that characterizes our employment of any of twenty-five leading therapeutic agents, including quinine, morphine, alcohol, strychnine, etc. Idiosyncrasies to these drugs are to be expected. If idiosyncrasies to antitoxine exist, their effects are confined to an occasional urticaria excited by an unripened serum. From the first, as the powers and limitation of antitoxine became better appreciated, the dose recommended was increased, and the interval in repetition decreased. As indicated in the recent report of the American Pædiatric Association, the further decrease in the mortality rate from diphtheria will depend upon the more general employment of concentrated antitoxines reasonably early, without fear, and in doses of one thousand or two thousand units, repeated when need be within ten or twelve hours. The best adjustment of dose at present recognized is briefly summed up as follows: In all ordinary cases of pharyngeal type give one thousand units immediately upon making the clinical diagnosis. If treatment is inaugurated late, or the type is laryngeal, or the case is one of membranous croup, give two thousand units. In every instance, if the disease is not arrested or the indications are that sufficient antitoxine has not been administered, repeat the dose, or give double the dose, within twelve hours.

582 FEDERAL STREET.

The New York Medical Journal.

A WEEKLY REVIEW OF MEDICINE.

EDITED BY

FRANK P. FOSTER, M.D.

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PUBLISHED BY

D. APPLETON & CO., 72 Fifth Avenue, New York.